

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2004/016336

| A. CLASSIFICATION OF SUBJECT MATTER Int.Cl ⁷ C12N15/09, A61K35/12, A61K35/76, C12N5/00, A61P35/00, C07K7/04, C07K14/705, C07K14/82, C07K16/30, C07K16/32, C07K19/00, C12N1/15, C12N1/19, C12N1/21, A61K38/04, C12P21/02 According to International Patent Classification (IPC) or to both national classification and IPC | | |
|--|---|--|
| B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) Int.Cl ⁷ C12N15/09, A61K35/12, A61K35/76, C12N5/00, C07K7/04, C07K14/705, C07K14/82, C07K16/30, C07K16/32, C07K19/00, C12N1/15, C12N1/19, C12N1/21, A61K38/04, C12P21/02 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched | | |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CA/MEDLINE/BIOSIS/EMBASE/BIOTECHABS/WPIDS (STN), GenBank/EMBL/DDBJ/ GeneSeq | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X Y | JP 2002-525099 A (Corixa Corp.), 13 August, 2002 (13.08.02), Pages 1, 2, 123, 124 & WO 00/18795 A | 1, 2 1, 2, 4, 5, 7-18, 20-23 |
| Y | Ozdemir, Enver; KAKEHI, Yoshiyuki; NAKAMURA, Eijiro; KINOSHITA, Hidefumi; TERACHI, Toshiro; OKADA, Yusaku; YOSHIDA, Osamu, HLA-DRB1*0101 and *0405 as protective alleles in Japanese patients with renal cell carcinoma., Cancer Research, (1997), Vol.57, No.4, pages 742 to 746 | 1, 2, 4, 5, 7-18, 20-23 |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | |
| * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family | | |
| Date of the actual completion of the international search 19 January, 2005 (19.01.05) | | Date of mailing of the international search report 08 February, 2005 (08.02.05) |
| Name and mailing address of the ISA/ Japanese Patent Office | | Authorized officer |
| Facsimile No. | | Telephone No. |

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|----------------------------|
| Y | Friede, Thomas; Gnau, Volker; Jung, Guenther; Keilholz, Wieland; Stevanovic, Stefan; Rammensee, Hans-Georg, Natural ligand motifs of closely related HLA-DR4 molecules predict features of rheumatoid arthritis associated peptides, Biochimicaet.Biophysica.Acta., (1996), 1316(2), 85-101 | 1, 2, 4, 5, 7-18, 20-23 |
| Y | Rammensee, Hans-Georg; Friede, Thomas; Stevanovic, Stefan, MHC ligands and peptide motifs; first listing, Immunogenetics (1995), 41(4), 178-228 | 1, 2, 4, 5, 7-18, 20-23 |

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 19, 24
because they relate to subject matter not required to be searched by this Authority, namely:
The inventions as set forth in claims 19 and 24 pertain to methods for treatment of the human body by therapy.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
(See extra sheet.)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
The parts relating to a peptide containing the amino acid sequence represented by SEQ ID NO:2 or an amino acid sequence derived therefrom by substitution(s) of amino acid residue(s) (continued to extra sheet)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

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Continuation of Box No.III of continuation of first sheet(2)

Since the peptide as set forth in claim 1 is not specified by chemical structure and, therefore, seemingly involves a great number of unspecified peptides. Based on the descriptions in claims 2, 4 and 5 depending on claim 1, it is understood that this peptide involves at least various peptides as set forth in claims 2, 4 and 5. Discussion on the various peptides as set forth in claims 2, 4 and 5 indicates that there is no amino acid sequence serving as a fundamental skeleton common to the peptides having the respective amino acid sequences represented by SEQ ID NOS:2 to 23 as set forth in claim 2, taking the amino acid sequences thereof into consideration. Among the peptides as set forth in claims 4 and 5, those having amino acid sequences derived from the respective amino acid sequences represented by SEQ ID NOS:2 to 23 by substitution(s) of amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) suffer from changes in the amino acids of the amino acid sequences containing the respective amino acid sequences represented by SEQ ID NOS:2 to 23. Thus, there is no amino acid sequence serving as a fundamental skeleton common to these peptides and the original peptides. Also, there is no amino acid sequence serving as a fundamental skeleton common to each other. Although the peptides according to the invention are common to each other in being a peptide comprising from 10 to 25 consecutive amino acids in the human WT1 amino acid sequence and binding to HLA-DRB1*0405 to induce helper T cells, unity of invention relating to peptides which are chemicals should be judged based on the chemical structures of the chemicals, i.e., the amino acid sequences of the peptides. Thus, the above common matter cannot be considered inherently as imparting unity of invention to the peptides according to the present invention. Moreover, the following document 1 reports a polypeptide involving its modification having the immunogenic moiety of native WT1 or one or more substitutions, deletions, additions and/or insertions. According to this report, such a modification suffers from no lowering in the ability to react with WT1-specific antiserum and/or T cell line or a clone thereof due to the modification and the above polypeptide contains 16 or less consecutive amino acid residues occurring in native WT1 polypeptide, binds to an MHC class II molecule and thus induces a helper T cell response (refer to document 1, pages 1, 2, 123, 124, etc.). Accordingly, being a peptide comprising 10 to 25 consecutive amino acids in the amino acid sequence of human WT1 and inducing helper T cells as described in the present invention cannot be considered as a special technical feature as specified in Patent Cooperation Treaty, Rule 13.2. Although document 1 refers nothing about being a peptide binding to HLA-DRB1*0405 as described in the present invention, the usefulness of the peptide according to the invention resides in being capable of inducing helper T cells. Namely, it appears that the usefulness does not depend on the subtype of the MHC class II molecule to which the peptide binds in the course of the induction. Thus, being a peptide binding to HLA-DRB1*0405 as described above cannot be considered as a special technical feature based on Patent Cooperation Treaty, Rule 13.2.

Based on the above findings, it will be discussed how many invention groups the present international application has. Concerning a peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:2 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s), histidine at the 4-position may be substituted by any of at least 6 amino acids, i.e., valine, isoleucine, leucine, methionine, aspartic acid and glutamic acid (continued to the next sheet)

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as described in claim 5, while aspartic acid at the 6-position may be substituted by any of at least 5 amino acids, i.e., serine, threonine, glutamine, lysine and aspartic acid as described in claim 5. That is, at least 30 (6x5) peptides are involved in total therein. Similarly, a peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:3 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 25 (5x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:4 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (5x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:5 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (6x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:6 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (6x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:7 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (6x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:8 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (6x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:9 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36 (6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:10 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36 (6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:11 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36 (6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:12 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (5x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:13 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30 (5x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:14 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 25 (5x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:15 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36 (6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:16 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36 (6x6) peptides in total. (continued to the next sheet)

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A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:17 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30(6x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:18 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36(6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:19 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 25(5x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:20 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36(6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:21 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30(6x5) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:22 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 36(6x6) peptides in total. A peptide having an amino acid sequence derived from the amino acid sequence represented by SEQ ID NO:23 by substitution of the amino acid residue(s) at the 4-position and/or the 6-positions by other amino acid residue(s) involves at least 30(6x5) peptides in total.

Accordingly, the present international application has 22 groups of peptides having the respective amino acid sequences represented by SEQ ID NOS:2 to 23 or amino acid sequences derived therefrom by substitution(s) at amino acid residue(s) at the 1-position and/or the 9-position by other amino acid residue(s) as set forth in claim 2, and at least 693 (30+25+30+30+30+30+30+36+36+36+30+30+25+36+36+30+36+25+36+30+36+30) groups of peptides having amino acid sequences derived therefrom by substitution(s) at amino acid residue(s) at the 4-position and/or the 6-position by other amino acid residue(s). It is to be concluded that these groups of peptides do not technically relate so as to form a single general inventive concept with the inventions according to claims 7 to 18 and 20 to 23 relating to the utilization of these groups of peptides and the peptides described therein and thus there are at least 715 (22+693) groups of inventions constructed thereby.

Document 1: International Patent Publication 2002-525099

Continuation of Box No.III-4 of continuation of first sheet(2)

at the 1- and/or 9-positions by other amino acid residue(s) in claims 1, 2, 4, 5, 7 to 18 and 20 to 23.

A. 発明の属する分野の分類 (国際特許分類 (IPC))

Int cl7 C12N 15/09 A61K 35/12 A61K 35/76 C12N 5/00 A61P 35/00 C07K 7/04 C07K 14/705 C07K 14/82 C07K 16/30 C07K 16/32 C07K 19/00 C12N 1/15 C12N 1/19 C12N 1/21 A61K 38/04 C12P 21/02

B. 調査を行った分野

調査を行った最小限資料 (国際特許分類 (IPC))

Int cl7 C12N 15/09 A61K 35/12 A61K 35/76 C12N 5/00 C07K 7/04 C07K 14/705 C07K 14/82 C07K 16/30 C07K 16/32 C07K 19/00 C12N 1/15 C12N 1/19 C12N 1/21 A61K 38/04 C12P 21/02

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

CA/MEDLINE/BIOSIS/EMBASE/BIOTECHABS/WPIDS (STN),
GenBank/EMBL/DDBJ/Geneseq

C. 関連すると認められる文献

| 引用文献の カテゴリー* | 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示 | 関連する 請求の範囲の番号 |
|-----------------|---|-------------------------------------|
| X Y | J P 2002-525099 A (コリクサ コーポレイション) 2002. 08. 13, 第1, 2, 123, 124頁他 & WO 00/18795 A | 1, 2 1, 2, 4, 5, 7-1 8, 20-23 |
| Y | Ozdemir, Enver; Kakehi, Yoshiyuki; Nakamura, Eijiro; Kinoshita, Hidefumi; Terachi, Toshiro; Okada, Yusaku; Yoshida, Osamu, HLA-DRB1*0101 and *0405 as protective alleles in Japanese patients with renal cell carcinoma., Cancer Research, (1997) Vol. 57, No. 4, pp. 742-746. | 1, 2, 4, 5, 7-1 8, 20-23 |

☒ C欄の続きにも文献が列挙されている。

☐ パテントファミリーに関する別紙を参照。

* 引用文献のカテゴリー

- 「A」 特に関連のある文献ではなく、一般的技術水準を示すもの
「E」 国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの
「L」 優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す)
「O」 口頭による開示、使用、展示等に関する文献
「P」 国際出願日前で、かつ優先権の主張の基礎となる出願

の日の後に公表された文献

- 「T」 国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの
「X」 特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの
「Y」 特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの
「&」 同一パテントファミリー文献

国際調査を完了した日

19. 01. 2005

国際調査報告の発送日

08.02.2005

国際調査機関の名称及びあて先

日本国特許庁 (ISA/J P)

郵便番号100-8915

東京都千代田区霞が関三丁目4番3号

特許庁審査官 (権限のある職員)

内藤 伸一

4 B

8615

電話番号 03-3581-1101 内線 3448

| C (続き) . 関連すると認められる文献 | | |
|-----------------------|--|-----------------------------|
| 引用文献の カテゴリー* | 引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示 | 関連する 請求の範囲の番号 |
| Y | Friede, Thomas; Gnau, Volker; Jung, Guenther; Keilholz, Wiel and; Stevanovic, Stefan; Rammensee, Hans-Georg, Natural ligands and motifs of closely related HLA-DR4 molecules predict features of rheumatoid arthritis associated peptides, Biochimica et Biophysica Acta (1996), 1316(2), 85-101 | 1, 2, 4, 5, 7-1 8, 20-23 |
| Y | Rammensee, Hans-Georg; Friede, Thomas; Stevanovic, Stefan, MHC ligands and peptide motifs: first listing, Immunogenetics (1995), 41(4), 178-228 | 1, 2, 4, 5, 7-1 8, 20-23 |

第Ⅱ欄 請求の範囲の一部の調査ができないときの意見 (第1ページの2の続き)

法第8条第3項(PCT17条(2)(a))の規定により、この国際調査報告は次の理由により請求の範囲の一部について作成しなかった。

1. ☒ 請求の範囲 19, 24 は、この国際調査機関が調査をすることを要しない対象に係るものである。つまり、

請求の範囲19, 24の発明は、治療による人体の処置方法に関するものである。

2. ☐ 請求の範囲 _____ は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、

3. ☐ 請求の範囲 _____ は、従属請求の範囲であってPCT規則6.4(a)の第2文及び第3文の規定に従って記載されていない。

第Ⅲ欄 発明の単一性が欠如しているときの意見 (第1ページの3の続き)

次に述べるようにこの国際出願に二以上の発明があるところの国際調査機関は認めた。

別紙参照

1. ☐ 出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求の範囲について作成した。
2. ☐ 追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。
3. ☐ 出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったため、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。

4. ☒ 出願人が必要な追加調査手数料を期間内に納付しなかったため、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。

請求の範囲1, 2, 4, 5, 7-18, 20-23のうち、配列番号: 2記載のアミノ酸配列を含有するか、又は、その第1位及び/若しくは第9位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有するペプチドに関する部分

追加調査手数料の異議の申立てに関する注意

- ☐ 追加調査手数料の納付と共に出願人から異議申立てがあった。
- ☒ 追加調査手数料の納付と共に出願人から異議申立てがなかった。

第Ⅲ欄の続き

請求の範囲1に記載されたペプチドは、化学構造によって特定されておらず、不特定多数のペプチドを包含するものと解されるが、請求の範囲1を引用する請求の範囲2、4、5の記載からみて、少なくとも、請求の範囲2、4、5に記載された種々のペプチドを包含するものと解される。そこで、請求の範囲2、4、5に記載された種々のペプチドについて検討すると、請求の範囲2に記載の配列番号：2～23のいずれか記載のアミノ酸配列を含有するものは、それらのアミノ酸配列からみて、互いに共通する基本骨格といえるアミノ酸配列を共有するものとはいえない。また、請求の範囲4、5に記載のペプチドのうち、配列番号：2～23のいずれか記載のアミノ酸配列の第4位および／または第6位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有するものは、各々、基になる、配列番号：2～23のいずれか記載のアミノ酸配列を含有するペプチドのアミノ酸配列の途中のアミノ酸が変化しているものであるから、該基になるペプチドとの間で、共通する基本骨格といえるアミノ酸配列を共有するものとはいえないし、互いの間でも、共通する基本骨格といえるアミノ酸配列を共有するものとはいえない。なお、本願発明のペプチドは、ヒトWT1のアミノ酸配列における連続する10～25アミノ酸からなるペプチドであって、HLA-DRB1*0405に結合してヘルパーT細胞を誘導するものである点で共通するが、化学物質であるペプチドの発明の単一性は、化学物質の化学構造、即ち、ペプチドのアミノ酸配列によって判断されるものであって、上記の点で共通することは、もとより本願発明のペプチドに発明の単一性をもたらすものとはいえないが、加えて、下記文献1には、ネイティブのWT1の免疫原性部分あるいは1以上の置換、欠失、付加および／または挿入において異なるその改変体を含む、ポリペプチドであって、このような改変により、該改変体のWT1特異的抗血清および／またはT細胞株もしくはクローンと反応する能力が実質的に減少しておらず、ここで該ポリペプチドは、ネイティブのWT1ポリペプチド内に存在する16以下の連続するアミノ酸残基を含み、MHCクラスII分子に結合し、ヘルパーT細胞応答を誘発し得るもの、が記載されている（文献1第1、2、123、124頁他参照）から、本願発明にいう、ヒトWT1のアミノ酸配列における連続する10～25アミノ酸からなるペプチドであって、ヘルパーT細胞を誘導するものである点は、特許協力条約に基づく規則13.2に規定する特別な技術的特徴であるとはいえない。また、文献1には、本願発明にいう、HLA-DRB1*0405に結合するペプチドである点についての記載は見いだせないが、本願発明のペプチドの有用性は、ヘルパーT細胞を誘導し得るものである点にあるのであって、該誘導の際、どのMHCクラスII分子のサブタイプに結合するかは、該有用性を別異のものとするほどの事柄であるとはいえないから、上記HLA-DRB1*0405に結合するペプチドである点も、特許協力条約に基づく規則13.2に規定する特別な技術的特徴であるとはいえない。

以上の認定を基に、本件国際出願にいくつの発明群が含まれるか検討する。まず、配列番号：2記載のアミノ酸配列の第4位および／または第6位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有するペプチドについてみると、第4位については、ヒスチジンが、少なくとも請求の範囲5に記載のバリン、イソロイシン、ロイシン、メチオニン、アスパラギン酸、グルタミン酸という6つのアミノ酸に置換し得、第6位については、アスパラギンが、少なくとも請求の範囲5に記載のセリン、スレオニン、グルタミン、リジン、アスパラギン酸という5つのアミノ酸に置換し得るから、少なくとも、合計 $6 \times 5 = 30$ とおりの、ペプチドを包含することになる。同様に、配列番号：3記載のアミノ酸配列の第4位および／または第6位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有するペプチドは、少なくとも、合計 $5 \times 5 = 25$ とおりの、ペプチドを包含することになり、配列番号：4記載のアミノ酸配列の第4位および／または第6位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有するペプチドは、少なくとも、合計 $5 \times 6 = 30$ とおりの、ペプチドを包含することになり、配列番号：5記載のアミノ酸配列の第4位および／または第6位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有するペプチドは、少なくとも、合計 $6 \times 5 = 30$ とおりの、ペプチドを包含することになり、配列番号：6記載のア

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[illegible]

したがって、本件国際出願においては、請求の範囲 2 に記載の配列番号：2～23 のいずれか記載のアミノ酸配列を含有するか、又は、その第 1 位及び／若しくは第 9 位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有する、

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22個のペプチド群、並びに、その第4位及び／又は第6位のアミノ酸残基が他のアミノ酸残基に置換されたアミノ酸配列を含有する、少なくとも $30+25+30+30+30+30+36+36+36+30+30+25+36+36+30+36+25+36+30+36+30=693$ 個のペプチド群が、各々、これらのペプチド群を用いる場合の請求の範囲7-18、20-23記載のペプチドなどの発明と共に、互いに、単一の一般的発明概念を形成するように連関しているものとはいえない、少なくとも $22+693=715$ 個の発明群を構成しているものといわざるを得ない。

文献1：特表2002-525099号公報